UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,910	07/15/2003	Yoshihiko Nishimura	81918.0003	7180

26021 7590 11/01/2004

HOGAN & HARTSON L.L.P.
500 S. GRAND AVENUE
SUITE 1900
LOS ANGELES, CA 90071-2611

EXAMINER	
KAM, CHIH MIN	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 11/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/619,910	NISHIMURA ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/15/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of SEQ ID NO:11 in the response filed August 12, 2004 is acknowledged. Therefore, claims 12-24 and SEQ ID NO:11 are examined. In the preliminary amendment filed July 15, 2003, a paper copy of substituted sequence listing was submitted and entered.

Claim Objections

2. Claims 12-14 are objected to because the claim contains recitation of non-elected amino acid sequences such as SEQ ID NOs:2, 3, 4, 5, 6, 7 and 8. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

3. Claims 12-17, 19, 22 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Oppermann *et al.* (WO89/09788).

Oppermann *et al.* teach a synthetic osteogenic protein comprising an amino acid sequence of OP1 peptide (102 amino acid residues), which contains the amino acid sequence of SEQ ID NO:11 at residues 57-76 (see attached amino acid sequence match), and can induce endochondral bone formation and bone marrow differentiation at the locus of the implant, when properly folded and implanted in a mammal in association with a matrix (pages 6 and 8; claims 12, 13, 15, 16 and 22); and the matrix is a biocompatible and biodegradable material such as demineralized xenogenic bone, collagen, homopolymers and coplymers of glycolic acid and lactic acid, hydroxypatite, tricalcium phosphate and other calcium phosphate (page 14, second paragraph-page 15, first paragraph; claim 17). The osteogenic protein can be prepared as active protein at pH 8 using Tris buffer containing Guanidine•HCl and dithiothreitol (page 30, second paragraph-page 31, first paragraph; claims 14, 19 and 24).

4. Claims 12- 22 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Rueger *et al.* (U.S. Patent 6,281,195, priority date Feb. 7, 1997).

Rueger *et al.* teach an osteogenic protein such as OP1 (431 residues; SEQ ID NO:2 of the patent; column 12, line 4), which contains the amino acid sequence of SEQ ID NO:11 at residues 386-405 (see attached amino acid sequence match), and can induce endochondral bone formation sufficient to repair critical-sized, segmental bone defects, when admixed with a biocompatible, amorphous non-rigid carrier as a matrix-free device, where the carrier can be alkylcelluloses, poloxamers, dextrins, sugars, lactose, mannitol, and physiological saline (PBS) (column 3, lines 30-67; column 10, line 42-column 11, line 11; column 16, line 40-column 17, line 11; claims 12-

17, 19, 20, 22 and 24). The osteogenic devices were made with 62.5 μg lyophilized OP-1 with 25 mg collagen matrix (0.0625 mg/25 mg = 0.25%; column 20, lines 11-60; claim 18), and the osteogenic devices in solution were prepared with a desired dose of OP-1 (5-25 mg) in 20 mM acetate buffer in a 100 μl injection volume (e.g., 5 mg/100 μl = 5 g/100 ml = 5%; column 21, lines 24-33; claim 21).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 12-17, 19 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oppermann *et al.* (WO89/09788) in view of Lipton (U.S. Patent 5,028,592).

Oppermann *et al.* teach a synthetic osteogenic protein comprising an amino acid sequence of OP1 (102 amino acid residues), which contains the amino acid sequence of SEQ ID NO:11 at residues 57-76 (see attached amino acid sequence match), and can induce endochondral bone formation and bone marrow differentiation at the locus of the implant, when properly folded and implanted in a mammal in association with a matrix (pages 6 and 8; claims 12, 13, 15, 16 and 22); and the matrix is a biocompatible and biodegradable material such as demineralized xenogenic bone, collagen, homopolymers and coplymers of glycolic acid and lactic acid, hydroxypatite, tricalcium phosphate and other calcium phosphate (page 14, second paragraph-page 15, first paragraph; claim 17). The osteogenic protein can be prepared as active protein at pH 8 using Tris buffer containing Guanidine•HCl and dithiothreitol (page 30, second

paragraph-page 31, first paragraph; claims 14, 19 and 24). However, Oppermann *et al.* do not disclose the peptide having N-terminal acetylated or C-terminal amidated. Lipton teaches a bioactive peptide is protected by an acetyl group at N-terminus or an amido group at C-terminus, and indicates the protected peptide is more active pharmacologically than the unprotected peptide because the protected peptide is less susceptible to acid hydrolysis or enzymatic attack and degradation (column 4, lines 56-66). At the time of invention was made, it would have been obvious that one of ordinary skill in the art is motivated to use the peptide comprising SEQ ID NO:11 taught by Oppermann *et al.* to prepare the protected peptide by amidation at C-terminal or acetylation at N-terminal as taught by Lipton (claim 23) because the peptide with N- or C-terminal protected would reduce its susceptibility to acid hydrolysis or enzymatic attack and degradation, and is more active pharmacologically than the unprotected peptide. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CMK
October 26, 2004